

**REMARKS**

Claims 1, 4-8, 11-15, 17, 18, 22 and 23 are pending in the application. Claims 17 and 18 are withdrawn from consideration. Claims 1-16, 19 and 20 are rejected.

Claims 1, 17 and 18 are amended. Claims 21-22 are added. Claims 2, 3, 9, 10, 16, 19, 20, and 21 are canceled.

Claim 1 has been amended to recite that CAP-18 is “native” CAP-18 and dependent claim 21 has been added to recite that CAP 18 consists of the amino acid sequence of SEQ ID NO:4, as supported at page 7, fourth and fifth full paragraphs.

Claim 1 has been amended to replace the word “protein” with the word “peptide,” and to replace “specifically reacts” with “specifically binds” to parallel the language used in the detailed description, as suggested by the Examiner.

Claim 1 has been amended to recite a further step of genotypically or phenotypically confirming the diagnosis, as supported by, for example, page 2, second full paragraph.

Claims 1, 17 and 18 have been amended to include the recitation of determination of the presence or absence of risk of or assessment of the level of the risk of cystic lung fibrosis and new claims 22 and 23 recite a method for assessment of severity and/or acuteness of or assessment regarding progress of cystic lung fibrosis as supported, for example, in the paragraph bridging pages 20 and 21.

Claim 1 has also been amended to recite that the biological sample is expectoration or bronchoalveolar lavage fluid, as was recited in claims 3 and 10, now canceled.

Claim 1 has been amended so that the correlating step indicates that an increase in the level of CAP 18 correlates with a diagnosis of cystic lung fibrosis. This amendment essentially makes claims 1 and 2 the same. Thus, claim 2 is canceled.

Further, because claim 2 has been canceled, all claims dependent there from have been amended to depend from claim 22.

**A. Claim Objections**

1. Claims 1-2 and 19-20 are objected to because of the following informalities:

The Examiner notes that the claims recite methods "for assessment of possibility of cystic lung fibrosis". The Examiner asserts that it appears that an article such as "the" is required before the word "possibility" in the claims.

The phrase has been removed from claim 1 and claims 2 and 19-20 are canceled, making the objection moot.

2. Regarding claims 19-20, the Examiner notes that the claims refer to both "CAP 18" and "CAP-18" (hyphenated). Applicant is requested to employ consistent spelling of this protein throughout the claims.

The specification does not hyphenate "CAP 18." Therefore, the claims have been amended, where appropriate, to remove the hyphen.

**B. Claim Rejections - Under 35 USC § 112, first paragraph, new matter**

Claims 1-16 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, as introducing new matter into the specification.

1. In paragraph 7, the Examiner asserts that the specification defines CAP 18 as not only the native protein, but also naturally occurring variants thereof and proteins having slight structural differences from native CAP 18. However, according to the Examiner, the specification does not teach any antibodies that bind to the naturally occurring variants or proteins having slight structural differences from native CAP 18. The Examiner further asserts that there is nothing in the record to indicate that proteins having structural differences from native CAP 18 would necessarily and always specifically react with antibodies that specifically react with proteins comprising SEQ ID NOs:1, 2 or 3 or consisting of SEQ ID NO: 4.

This rejection is overcome by amending claim 1 and other claims, where relevant, to recite that the CAP 18 is “native” CAP-18.

2. In paragraph 8, the Examiner asserts that use of the word “protein” in the amendments to claims 1 and 2 is new matter, because the specification only refers to “peptides.” The Examiner asserts that proteins and peptides are not the same.

The claims have been amended to replace the word “protein” with the word “peptide.”

3. In paragraph 9, the Examiner asserts that use of the phrase “specifically reacts” in the amendments to claims 1 and 2 is new matter, because the specification only refers to “specifically binds.” The Examiner asserts that reacting and binding are not necessarily the same.

The claims have been amended to replace “specifically reacts” with “specifically binds.”

4. In paragraph 10, the Examiner asserts that there is no support in the specification for the amendments to claims 1 and 2 that recite antibodies to a protein having the amino acid

sequence of SEQ ID NO:4. The Examiner asserts that even though SEQ ID NO:4 includes SEQ ID NOs:1, 2 and 3, it also includes sequences not present in SEQ ID NOs:1, 2 or 3, and the specification does not disclose antibodies that react with these regions of SEQ ID NO:4.

This aspect of the rejection is moot in view of the amendments to claim 1 deleting the allegedly unsupported subject matter.

5. In paragraph 11, the Examiner asserts that claims 19 and 20 introduce new matter into the specification because describing CAP 18 as “having” the amino acid sequence of SEQ ID NO:4 includes proteins that have sequences on either or both ends of SEQ ID NO:4. However, the Examiner asserts that there is no support for measuring a protein that has such additional sequences.

This aspect of the rejection is overcome by amending claims that refer to SEQ ID NO:4 as “consisting of” instead of “having,” the amino acid sequence thereof.

**C. Claim Rejections - Under 35 USC § 112, first paragraph, written description**

Claims 1-16 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, as lacking written description in the specification. According to the Examiner, the specification does not adequately define all possible CAP-18 proteins falling within the definition given at page 7, last full paragraph of the specification.

This rejection is overcome by amending the claims to recite that the CAP 18 measured is the “native” CAP 18 or CAP 18 “consisting of SEQ ID NO:4.”

**D. Claim Rejections - Under 35 USC § 112, first paragraph, enablement**

Claims 1-16 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

1. The Examiner asserts that an increased level of CAP 18 is not specific to cystic lung fibrosis. In support, the Examiner cites Xiao et al. and Applicant's copending application 2006/00571134. Thus, the Examiner concludes that just measuring the level of CAP 18 cannot, by itself, diagnose cystic lung fibrosis.

This aspect of the rejection is overcome by amending the claims to recite a further step of genotypically or phenotypically confirming the diagnosis.

2. The Examiner asserts that the specification does not enable measuring all proteins within the genus of "proteins having slight structural differences from native (non-mutated) CAP 18 but exhibiting no significant differences in function, behavior, etc."

This aspect of the rejection is overcome by amending the claims to recite that the CAP 18 that is measured is "native" CAP 18 or CAP 18 that "consists of the amino acid sequence of SEQ ID NO:4."

3. The Examiner asserts that the claims are not enabled for any biological sample. In support, the Examiner cites Applicant's own publication, Xiao et al. as teaching that there is no difference in CAP 18 levels in healthy vs. disease populations.

This aspect of the rejection has been overcome by amending the claims to recite that the biological sample is expectoration or bronchoalveolar lavage fluid.

**E. Claim Rejections - Under 35 USC § 112, second paragraph**

Claims 1-16 and 19-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claims 1 and 2 are allegedly indefinite for use of the term “CAP 18.” The Examiner asserts that as defined in the specification, one skilled in the art would not know whether they were practicing within or outside of the claims.

Similarly, claims 19-20 are allegedly indefinite for using the language CAP 18 “having” the amino acid sequence of SEQ ID NO:4, as this language includes proteins having additional amino acids at the amino and/or carboxyl termini.

This rejection is overcome by amending claim 1 to recite that the CAP 18 that is measured is “native” CAP 18 or that it “consists of” the amino acid sequence of SEQ ID NO:4.

**F. Claim Rejections - Under 35 USC § 102**

1. Claims 1-7 and 10-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Bals et al. ("Salt-Independent Abnormality of Antimicrobial Activity in Cystic Fibrosis Airway Surface Fluid" Am. J. Respir. Cell Mol. Biol. 25 (2001), p. 21-25) and in light of the evidence of iHOP (Information Hyperlinked over Proteins — data for CAMP, cathelicidin antimicrobial peptide, p. 1, downloaded from <http://www.ihop-net.org/UniPub/iHOP/gs/86912.html> on 01/04/2007) and Larrick et al. ("Human CAP18: a Novel Antimicrobial Lipopolysaccharide-Binding Protein" Infection and Immunity 63 91995), 1291-1297), for the reasons set forth in the prior Office Action.

While breadth does not necessarily make a claim indefinite, in order to further prosecution, claim 1 has been amended so that the correlating step indicates that an increase in the level of CAP 18 correlates with a diagnosis of cystic lung fibrosis

**G. Claim Rejections - Under 35 USC § 103**

Claims 8 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bals et al. in light of iHOP and Larrick, and in view of Weinberg et al. (US 6,187,536 B 1), for the reasons set forth in the prior Office Action. In paragraph 26 of the Office Action, the Examiner states that although he agrees that Bals et al. teaches away from diagnosis of cystic fibrosis, the claims recite a much broader purpose.

This rejection is overcome by amending claim 1 so that the correlating step indicates that an increase in the level of CAP 18 correlates with a diagnosis of cystic lung fibrosis

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.


Respectfully submitted,

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Date: October 11, 2007